Acute Respiratory Infections Panels

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Guidelines

Acute Respiratory Infections Panels

The acute respiratory infections (ARI) collectively represent the most common infections of mankind. Illnesses vary from mild to severe, and the consequences range from minor functional impairment to death. All population groups in all geographic locations are affected. In developed society, these infections are a major medical problem, and an increase in their relative significance characterizes the transition from a developing country to a developed country. ARI are major areas of medical research in both the United States and Japan.

Acknowledgment of the medical significance and the mutual research interests of the United States and Japan led to the creation of the Acute Respiratory Diseases Panels of the U.S.-Japan Cooperative Medical Science Program in 1997. The goals of the ARI Panels are as follows:

- To understand the etiology and long-term health effect of ARI in the United States, Japan, and Pacific Rim countries
- To stimulate basic research that may lead to new information on the pathogenesis, immunity, and functional components of the pathogens that cause ARI
- To conduct research and development on vaccines and therapeutic agents targeted against the various respiratory pathogens

Three Year Summary

Broad Goals

The operational guidelines for the ARI Panel program were developed during and after the initial meeting of the Panels in Nagasaki, Japan, in March 1997. Annual meetings are held for the exchange of information and to identify mutual scientific interests, which are used as a basis for establishing cooperative programs. The Panels serve as a forum (1) to coordinate an exchange program that involves scientific contacts, visiting scientists, and efforts to meet the needs of individual investigators (2) to promote interactions with Japanese and U.S. industry to develop vaccines and therapeutic agents for prevention and treatment of ARI. To accomplish identified objectives, the Panels establish working group subcommittees to address specific problems related to ARI and each subcommittee then creates its own research agenda.

Research options have been identified for each major ARI goal (see Guidelines). Assessment of the etiology and long-term health impact of ARI includes microbiological, clinical, and, epidemiologic studies in the United States, Japan, and Pacific Rim countries and quantitation of the emerging role of ARI in developing countries. Options for basic research include studies of mucosal immune responses and immunity, pathogenesis, and new approaches to diagnosis and vaccine development. Options for research and development of vaccines and therapeutic agents include (1) assessment of the patterns of resistance to, antimicrobial agents and development of strategies to prevent the emergence of antimicrobial resistance and determination of the impact of diseases that are preventable using available vaccine in the United States and Asia and creation of public health vaccination programs to prevent these diseases, as appropriate.

Progress and Accomplishments

At the inaugural meeting of the ARI Panels in Nagasaki, the impact of ARI was emphasized, and the array of agents causing ARI were discussed. These agents included *Bordetella pertussis, Mycoplasma pneumoniae, Haemophilus influenzae* (type B and nontypeable strains), *Streptococcus pneumoniae*, group B streptococci, respiratory syncytial virus, measles virus, and parainfluenza and influenza. Numerous options for cooperation between scientific investigators and research and health policy administrators in the United States and Japan were considered. All options were in accordance with and supportive of the terms of agreement for the ARI Panel programs.

Because of the broad array of significant infectious agents to be addressed, the Panels instituted the subcommittee approach for assessing and developing programs for research on ARI. The initial focus of the Panels has been on influenza, a major, country-wide and global respiratory disease. Cooperative efforts on influenza constitute the primary accomplishments of the 3-year period since the Panels were formed. A second subcommittee is beginning to develop a program of research that focuses on the major bacterial causes of ARI, especially pneumococci, *H. influenza* (type B and nontypeable), and *Moraxella catarrhalis*.

Influenza Subcommittee

In the inaugural meeting of the Influenza Subcommittee in San Francisco, California, in September 1997, two major programs for cooperation were established.

Surveillance

A cooperation on Asian and global human influenza surveillance was developed by two Panel members who direct the World Health Organization (WHO) influenza reference laboratories in the United States and Japan. This collaboration included exchange of information and personnel and joint educational programs in China to improve the capability for surveillance there.

Inactivated Vaccines

Cooperative efforts were developed to promote a strategic plan for use of vaccines containing inactivated viruses to control the serious consequences of influenza in Japan, during the interpandemic periods.

The importance of surveillance of influenza in Asia was emphasized by experience with the influenza A (H5N1) in Hong Kong, China, in 1997, and was reemphasized in 1999 with the isolation of influenza A (H9N2) virus from two sick children in Hong Kong. The prevailing hypothesis is that most new pandemic strains of influenza may arise in China and that they derive genes from influenza viruses in the migratory bird population. To this end, the ARI Panels have been active in establishing cooperative surveillance of animal influenza viruses in Asia. The program in Japan focuses on migratory birds in northern Asia and on swine in Taiwan, and the U.S. program involves surveillance of migratory birds that carry influenza virus in North America. A laboratory has been established in Hong Kong to study avian influenza viruses in that area and for exchange of viruses and reagents among investigators. Because of the extreme importance of this program and the progress being made in cooperation, it was desig-

nated as a Program of Excellence for the ARI Panels under the U.S.-Japan Cooperative Medical Science Program.

The ARI Panels have also promoted joint U.S.-Japan efforts to develop a coordinated and improved surveillance program of human influenza in China. A component of the interaction has been increased exchange of viruses and antisera between the WHO influenza centers in the United States and Japan. Scientists from Japan have visited the Centers for Disease Prevention and Control, Atlanta, Georgia, for training and exchange of information. In addition, collaborative efforts are under way with China to improve surveillance, as a component of the WHO worldwide influenza surveillance program. The WHO influenza centers in the United States and Japan are the primary sources of expertise for this effort.

Scientific exchanges at the annual meetings and at the 4th International Conference on Emerging Infectious Diseases in the Pacific Rim, in Bangkok, Thailand, March 2-4,1998, included discussions of vaccines containing inactivated influenza virus (inactivated influenza vaccines) and their demonstrated efficacy in developed countries. In the past, Japanese health policy for inactivated influenza vaccines was to vaccinate all schoolchildren in an effort to prevent epidemics of influenza. Since the epidemics continued, the policy was withdrawn in 1994 by the Ministry of Health. Subsequently, the use of inactivated vaccines in Japan fell to extremely low levels. The ARI Panels have participated in restoring confidence in inactivated vaccines among the public health authorities in Japan and supporting moves toward implementation of a policy to provide inactivated vaccines to persons as high risk for severe complications from influenza. This policy is prevalent in most developed countries. To further support his effort, a press conference took place at the annual Panel meeting in Kyoto, Japan, in March ,1999. In the following months, the Ministry of Health established a policy of recommending inactivated influenza vaccine for all elderly in Japan, and financial support was provided for implementation of the policy. The Ministry of Health is moving to ensure the availability of vaccine.

Bacterial Infections Subcommittee

The inaugural meeting of the Bacterial Infections Subcommittee was held in conjunction with the annual ARI Panel meeting, in February 2000, San Antonio, Texas. A program of research options was discussed, and plans were made to implement these options. The initial focus includes the following research areas:

- Assessment of the comparative use of antimicrobial agents in the United States and Japan, in relation to the development of patterns of resistance to these agents, and consideration of appropriate intervention strategies.

- Investigation of the impact of disease that is preventable with use of currently available vaccine (H. *influenza* B and pneumococci), in the United States and Japan

- Cooperative research on nontypeable *H. influenzae*, including analysis of types of strains circulating and evaluation of vaccine candidates

- Coordinated sharing of research tools, techniques, and training of young investigators

Future Goals

Future goals are as follows:

- Continue cooperative efforts on surveillance of animal influenza in Asia and North America through the ARI Panels' Program of Excellence in Animal Influenza

- Cooperate with WHO and other agencies and organizations to expand global surveillance of animal influenza

- Continue collaborative efforts to improve surveillance of human influenza in China and other Pacific Rim countries

- Determine the impact of influenza in developing countries of the Pacific Rim, where information is lacking, and promote application of control measures as appropriate

- Support expanded application of inactivated influenza virus vaccines in Japan and other Asian countries to include all high-risk groups, as recommended by the United States and WHO Advisory Committee on Immunization Practices (ACIP)

- Develop comparative assessments of use of antimicrobial agents and resistance to these agents, in the United States and Japan, and create intervention strategies for prevention

- Determine the impact of diseases for which vaccines are available, in Japan and other Pacific Rim countries

- Continue the assessment of the role of nontypeable *Haemophilus. influenzae* and *Moraxella catarrhalis* in disease, including studies on pathogenesis and options for vaccine development

- Develop cooperative programs to assess the status and research

needs of other infectious agents that cause acute ARI but are not currently under study

- Create cooperative programs for improved diagnosis and therapeutic interventions for ARI

- Develop cooperative research programs on approaches for development of vaccines for ARI

- Support and conduct basic research on the agents that cause ARI, including their molecular aspects, pathogenesis of disease, epidern-iology, and options for intervention for control

- Collaborate on developing human resources to support the cooperative medical research program

Selected References

United States

Cox NJ, Subbarao K. Global epidemiology of influenza: past and present. *Annu Rev Med* 2000;51:407-21

Ito T, Nelson J, Couceiro, SS, Kelm S, Baum LG, Krauss S, Castrucci MR, Donatelli I, Kida H,
Paulson JC, Webster RG, Kawaoka Y. Molecular basis for the generation in pigs of influenza A viruses with pandemic potential. *J Virol* 1998,72:7367-73

Klimov A, Simonsen L, Fukuda K, Cox N. Surveillance and impact of influenza in the United States. *Vaccine* 1999;17:S42-S46

Shortridge KF, Zhou NN, Guan Y, Gao P, Ito T, Kawaoka Y, Kodihalli S, Krauss S, Markwell D, Murti KG, Norwood M, Senne D, Sims L, Takada A, Webster RG. Characterization of avian H5NI influenza viruses from poultry in Hong Kong. *Virology* 1998;252:331-42

Simonsen L, Clarke MJ, Stroup DF, Williamson GD, Arden NH, Cox NJ. A method for timely assessment of influenza-associated mortality in the United States. *Epidemiology* 1997;8:390-5

Japan

Hiromoto Y, Saito T, Lindstrom SE, Li Y, Nerome F, Sugita S, Shinjoh M, Nerome K. Phylogenetic analysis of the three polymerase genes (PB 1, PB2, and PA) of influenza B virus. *J Gen* Prol 2000;81:929-37

Ito T, Kawaoka, Y, Vines A, Ishikawa H, Asai T, Kida H. Continued circulation of reassortant HIN2 influenza viruses in pigs in Japan. *Arch Virol* 1998;143:1773-82

Lindstrom SE, Hiromoto Y, Nishimura H, Saito T, Nerome R, Nerome K. Comparative analysis of evolutionary mechanisms of the hemagglutinin and three internal protein genes of influenza B virus: multiple cocirculating lineages and frequent reassortment of the NP, M, and NS genes. *J Prol* 1999;73:4413-26

Maeda H, Wu J, Okamoto T, Maruo K, Akaike T. Kallikrein-kinin in infection and cancer. *Immunopharmacology* 1999-43:115-28

Takada A, Kuboki N, Okazaki K, Ninomiya AI, Tanaka H, Ozaki H, Itamura S, Nishimura Enami M, Tashiro M, Shortridge KF, Kida H. Avirulent avian influenza virus as a vaccine strain against a potential human pandemic. *J Virol* 1999;73:8303-7